REMARKS

Entry of this Amendment is proper under 37 C.F.R. § 1.116, because the Amendment places the application in condition for allowance for the reasons discussed herein; does not introduce any new claims; does not raise any new issue requiring further search and/or consideration because the amendments amplify issues previously discussed throughout prosecution, and places the application in better form for an appeal should an appeal be necessary.

As stated in the Office Action Summary, claims 1, 3-8 and 10-39 are pending. Claims 1, 17, 18, 21 and 30 are amended herein. Claims 3-8, 10-12 and 20 are canceled herein. Applicants reserve the right to file at least one continuation or divisional application directed to any subject matter canceled by way of the present Amendment.

Claim 1 is amended herein to recite that the target cells are retina cells, and to recite specific target genes. Claims 17, 18, 21 and 30 are amended to correspond with amended claim 1. Basis for these amendments may be found throughout the specification and claims as-filed, especially at claim 10, Figure 1 and page 12, lines 24-30. No new matter is presented herein.

Claim Objections

Claim 1 stands objected because "calls" is purportedly misspelled. Claim is amended herein to recite “cells”. Thus, this objection is obviated.

Claim 6 stands objected to because "Watson-Crick's" is purportedly misspelled. Claim 6 is canceled herein. Thus, this rejection is moot.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1, 3-8, 10-12, 17, 18, 20, 21, 30 and 39 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite. Claims 1, 3-8, 10-12, 17, 18, 20, 21, and 30 are purportedly indefinite for the recitation of "non-animal or human eye tissue". To clarify this point, the claims are amended herein to recite human animal and non-human animal tissue.

Claims 7, 8, 11, 12, 30, and 39 are rejected because it is purportedly unclear whether the blocks of 2'O-methyl RNA flank only the stretch of DNA, or whether the poly(T) hairpin loops and G-C claim must be flanked as well. Claims 7-8 and 11-12 are canceled herein. Claim 30 is amended herein to clarify the claimed subject matter. Thus, this rejection is obviated.

Claims 30 and 39 stand rejected for the recitation of a nucleotide or nucleotides invented to revert an eye disease causing mutation, as this is purportedly confusing. Claim 30 is amended herein to clarify the claimed subject matter. Claims 30 and 39 are also purportedly indefinite for the recitation of "said at least part" without antecedent basis. Claim 30 is amended to provide antecedent basis. Claim 39 depends on claim 30, this rejection is obviated.

Claim 39 stands rejected as it is purportedly unclear if Applicant intends to claim the pharmaceutical composition comprising the oligonucleotide of claim 30, or whether the claimed oligonucleotide need only contain some portion of the DNA and 2'methoxy RNA of the oligonucleotide of claim 30. Applicants note that claim 30, from which claim 39 depends, is amended herein to recite a chimeric oligonucleotide having the sequence of SEQ ID NO:3, clarifying claim 39. Thus, this rejection is obviated.

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1, 3-8, 10-12, 17, 18, 20, 21, 30, and 39 stand rejected under 35 U.S.C. § 112, first paragraph, as purportedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse.

On page 5 of the Office Action, the Examiner notes that claims 10, 17, 18, 30, and 39 "limit the identity of the target gene, while claims 1, 3-8, 11, 12, 20, and 21 do not". Applicants note that the claims are amended herein to recite specific target genes, *i.e.*, cGMP phosphodiesterase, beta-subunit, RP1, opsin and HIF1α genes, as with claims 10, 17, 18, 30 and 39.

Further, the Office Actions states that at the time of filing, the legitimacy of using chimeraplasts to modify nucleic acid sequences was in doubt. The Office Action states that further evidence is required showing the skilled artisan, at the time of the invention, could use the claimed invention to revert mutations of eye tissue *in vivo*. In light of the amendments to the claims herein, Applicants refer to the Examples of the specification, on pages 21-26, setting forth *in vivo* examples using the cGMP phpsphodiesterase beta subunit. Further, by way of explanation, Applicants submit two references "Genplast y in the retina of the rd1 mouse" and "Recent advances in ocular drug delivery". Applicants further submit John B. Davies, et al., "Delivery of several forms of DNA, DNA-RNA hybrids, and dyes across human sclera by electrical fields," *Molecular Vision*, 9:569-578 (2003). These references show that retina disease causing mutations can be treated upon intravitreal injection with RNA-DNA hybrid oligonucleotide or single-stranded DNA, in combination with

iontophoresis to enhance penetration. Thus, Applicants submit that reversion of retina disease causing mutations can be accomplished using in mammals, as disclosed in the presently claimed invention, using the methods of the present invention.

The Office Action further states that claim 5 fails to establish a nexus between the "said target gene" and "a target gene" which has its expression product modified. To this end, Applicants note that claim 5 has been canceled herein.

Finally, with regard to claim 20, the Office Action states that U.S. Patent No. 6,001,088, on which the specification depends for description of this embodiment, teaches that needle and pad electrodes are alternative forms of electrodes, and it does not disclose a combination needle and pad electrode. To this end, Applicants note that claim 20 has been canceled herein. In light of the above remarks and amendments, Applicants submit the claims are enabled.

Claims 1, 3-7, 11, 12, 20, and 21 stand rejected under 35 U.S.C. § 112, first paragraph, as purportedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Office Action states that the specification discloses chimeric oligonucleotides designed to revert mutations in cGMP phosphodiesterase beta subunit, RP1, opsin, and HIF1alpha, but that the genus of mutated genes responsible for an inherited pathology is larger than this group. Applicants note that the claims are amended herein to recite specific target genes, *i.e.*, cGMP phosphodiesterase, beta-subunit, RP1, opsin and HIF1α genes. Thus, Applicants submit that sufficient written description is present, as stated by the Office Action.

Thus, Applicants request the rejections under 35 U.S.C. § 112, first paragraph, be withdrawn.

CONLCUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

In the event any further fees are due to maintain pendency of this application, the Examiner is authorized to charge such fees to Deposit Account No. **02-4800**.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: March 18, 2004

By: _____
Deborah H. Yellin
Registration No. 45,904

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620